## **AMENDMENTS TO THE CLAIMS**

1. (previously presented): A method for the isolation and purification of a compound having the formula

wherein R is cyano, halogen,  $CF_3$ - $(CF_2)_n$ - $SO_2$ -O-, -CHO, -CH<sub>2</sub>NO<sub>2</sub>, -CH<sub>2</sub>Cl, -CH<sub>2</sub>Br, -CH<sub>3</sub>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, or a group of formula

(VII), wherein

n is 0-8,

 $R^6$  and  $R^7$  are independently selected from optionally substituted  $C_{1\text{-}6}$ -alkyl, optionally substituted aryl- $C_{1\text{-}6}$ -alkyl, and optionally substituted aryl,

Z' in formula (VII) is O or S,

 $R^8$  and  $R^9$  are independently hydrogen or  $C_{1\text{-}6}$ -alkyl or  $R^8$  and  $R^9$  together form a  $C_{2\text{-}}$ 5-alkylene chain thereby forming a spiro ring,

R<sup>10</sup> is hydrogen or C<sub>1-6</sub>-alkyl, and

 $R^{11}$  is hydrogen,  $C_{1-6}$ -alkyl, a carboxy group, or a precursor group thereto, or  $R^{10}$  and  $R^{11}$  together form a  $C_{2-5}$ -alkylene chain thereby forming a spiro ring, the dotted line represents a double or single bond, Hal is halogen,

Z is a dimethylaminomethyl group, -CH<sub>2</sub>-L, -CH<sub>2</sub>-NO<sub>2</sub>, cyano, aldehyde, -CH<sub>2</sub>-O-Pg, -CH<sub>2</sub>-NPg<sub>1</sub>Pg<sub>2</sub>, -CH<sub>2</sub>-NMePg<sub>1</sub>, -CO-N(CH<sub>3</sub>)<sub>2</sub>, -CH(A<sup>1</sup>R<sup>12</sup>)(A<sup>1</sup>R<sup>13</sup>), -(A<sup>1</sup>R<sup>14</sup>)(A<sup>2</sup>R<sup>15</sup>)(A<sup>3</sup>R<sup>16</sup>), -COOR<sup>17</sup>, or -CH=CH-R<sup>18</sup>, wherein

Pg is a protection group for an alcohol group,

Pg<sub>1</sub> and Pg<sub>2</sub> are each independently a protection group for an amino group,

 $R^{12}$  and  $R^{13}$  are independently  $C_{1-6}$ -alkyl,  $C_{2-6}$ -alkenyl,  $C_{2-6}$ -alkynyl, or an optionally alkyl-substituted aryl or aralkyl group, or  $R^{12}$  and  $R^{13}$  together form a chain of 2 to 4 carbon atoms,

each of  $R^{14}$  -  $R^{18}$  are independently  $C_{1\text{-}6}$ -alkyl,  $C_{2\text{-}6}$ -alkenyl,  $C_{2\text{-}6}$ -alkynyl, or optionally  $C_{1\text{-}6}$ -alkyl-substituted aryl or aryl- $C_{1\text{-}6}$ -alkyl,

A<sup>1</sup>, A<sup>2</sup> and A<sup>3</sup> are independently O or S, and L is a leaving group,

W is O or S,

Y is a bond, O, S or NH,

and  $R^1$  is  $C_{1-10}$ -alkyl,  $C_{2-10}$ -alkenyl or  $C_{2-10}$ -alkynyl all of which may optionally be substituted with one or more substituents selected from  $C_{1-10}$ -alkoxy,  $C_{1-10}$ -alkylthio, halogen, nitro, cyano, di- $(C_{1-10}$ -alkyl)amino, aryl, aryloxy, arylthio and heteroaryl, or  $R^1$  is aryl, wherein any of the aryl and heteroaryl groups may optionally be substituted one or more times with substituents selected from  $C_{1-10}$ -alkyl,  $C_{2-10}$ -alkenyl,  $C_{2-10}$ -alkynyl,  $C_{1-10}$ -alkoxy,  $C_{1-10}$ -alkylthio, halogen, nitro, cyano, and di- $(C_{1-10}$ -alkyl)amino, or a salt thereof,

## and/or a diol of formula

wherein R, Z, Hal and the dotted line are as defined above, or a salt thereof, from a mixture containing the compound of formula (IV) and the diol of formula (II), comprising:

a) reacting said mixture containing the compound of formula (IV) and the diol of formula (II) with a cyclic anhydride or imide of formula

wherein X is  $-(CHR''')_{n}$ , wherein n is 0-2;

and R', R'', and R''' are independently selected from hydrogen,  $C_{1-6}$ -alkyl,  $C_{1-6}$ -alkoxy, aryloxy,  $C_{1-6}$ -acyloxy, and aryl-CO-O, wherein each aryl may be substituted with  $C_{1-6}$ -alkyl, or R' and R'' in an anhydride of formula (Ia) together are -O-CR $^4$ R $^5$ -O-, wherein R $^4$  and R $^5$  are independently hydrogen or  $C_{1-6}$ -alkyl, or R' and R'' in an anhydride of formula (Ib) are adjacent and together with the two carbon atoms to which they are attached form a benzene ring;

one of Q1 and Q2 is nitrogen and the other is carbon, or both are carbon;

A is  $C_{1-6}$ -alkylene, phenylene, or naphthylene wherein the  $C_{1-6}$ -alkylene, phenylene, or naphthylene groups may optionally be substituted one or more times with  $C_{1-6}$ -alkyl;

to form a mixture of the compound of formula (IV) and an ester having the formula

wherein R, Z and Hal are as defined above and V is -CHR'-X-CR''-COOH, -X-CHR''-CO-NH-A-COOH, - CHR''-X-CO-NH-A-COOH,

$$R' Q^{2} R''$$
 or  $R' Q^{2} R''$  COOH

wherein R', R", X, and A are as defined above;

- b) separating the compound of formula (IV) from the ester of formula (V) by a method selected from the group consisting of:
- i) allowing the acid of formula (V) or a salt thereof to precipitate from the reaction mixture, and separating the precipitate of the compound of formula (V) or a salt thereof from the reaction mixture, optionally followed by isolation of the compound of formula (IV) or a salt thereof from the reaction mixture;
- ii) partitioning between an organic solvent and an aqueous solvent whereby the compound of formula (IV) will be dissolved in the organic phase whereas the compound of formula (V) will be dissolved in the aqueous phase, separating the phases, and optionally isolating the compound of formula (IV) or a salt thereof and/or isolating the compound of formula (V) or a salt thereof; and
- iii) adsorbing the compound of formula (V) on a basic resin, separating the solvent containing the compound of formula (IV) from the resin, desorbing the compound of formula (V) from the basic resin, and optionally isolating the compound of formula (IV) or a salt thereof and/or isolating the compound of formula (V) or a salt thereof.
- 2. (previously presented): The method according to claim 1, wherein the separation of the compound of formula (IV) from the ester of formula (V) is performed by allowing the acid of formula (V) or a salt thereof to precipitate from the reaction mixture, and separating the precipitate of the compound of formula (V) of a salt thereof from the reaction mixture, optionally followed by isolation of the compound of formula (IV) or a salt thereof from the reaction mixture.

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3. (previously presented): The method according to claim 1, wherein R', R'', and R''' are independently selected from hydrogen and  $C_{1-6}$ -alkyl, and  $Q^1$  and  $Q^2$  are both carbon.

- 4. (previously presented): The method according to claim 1, wherein the S-enantiomer of the compound of formula (V) or a mixture of enantiomers of the compound of formula (V) comprising more than 50% of the S-enantiomer of the compound of formula (V) is separated from the R-enantiomer of the acyl derivative of formula (IV) or from a mixture of enantiomers of the acyl derivative of formula (IV) comprising more than 50% of the R-enantiomer of the acyl derivative of formula (IV).
- 5. (original): The method according to claim 4 wherein the S-enantiomer of the compound of formula (V) is separated from the R-enantiomer of the acyl derivative of formula (IV) or from a mixture of enantiomers of the acyl derivative of formula (IV) comprising more than 50% of the R-enantiomer of the acyl derivative of formula (IV).
- 6. (original): The method according to claim 5 wherein the S-enantiomer of the compound of formula (V) is separated from the R-enantiomer of the acyl derivative of formula (IV).
- 7. (previously presented): The method according to claim 1, wherein the S-enantiomer of the acyl derivative of formula (IV) or a mixture of enantiomers of the acyl derivative of formula (IV) comprising more than 50% of the S-enantiomer of the acyl derivative of formula (IV) is separated from the R-enantiomer of the compound of formula (V) or from a mixture of enantiomers of the compound of formula (V) comprising more than 50% of the R-enantiomer of the compound of formula (V).
- 8. (original): The method according to claim 7 wherein the S-enantiomer of the acyl derivative of formula (IV) is separated from the R-enantiomer of the compound of formula (V) or from a mixture of enantiomers of the compound of formula (V) comprising more than 50% of the R-enantiomer of the compound of formula (V).
- 9. (original): The method according to claim 8 wherein the S-enantiomer of the acyl derivative of formula (IV) is separated from the R-enantiomer of the compound of formula (V).

10. (currently amended): The method according to claim 4, wherein the compound of formula (V) is obtained in the form of the S-enantiomer, and wherein R is optionally converted to cyano, Z is optionally converted to a dimethylaminomethyl group, Hal is optionally converted to fluoro, and/or a dotted line representing a double bond is optionally converted to a single bond, in any order, followed by conversion of the compound of formula (V) to escitalopram or a derivative thereof having the formula

wherein R, Z and Hal are as defined above <u>provided that Z is not cyano</u>, by treatment with a base, optionally followed by, in any order, conversion of R to a cyano group, conversion of Z to a dimethylaminomethyl group, conversion of Hal to fluoro, and conversion of a dotted line representing a double bond to a single bond; optionally followed by conversion of escitalopram or a derivative of formula (VI) to a salt thereof.

11. (currently amended): The method according to claim 7, wherein the compound of formula (IV) is obtained in the form of the S-enantiomer, and wherein R is optionally converted to cyano, Z is optionally converted to a dimethylaminomethyl group, Hal is optionally converted to fluoro and/or a dotted line representing a double bond is optionally converted to a single bond, in any order, followed by conversion of the compound of formula (IV) to escitalopram or a derivative thereof having the formula

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wherein R, Z and Hal are as defined above <u>provided that Z is not cyano</u>, by treatment with a base, optionally followed by, in any order, conversion of R to cyano, conversion of Z to a dimethylaminomethyl group, conversion of Hal to fluoro, and conversion of a dotted line representing a double bond to a single bond; optionally followed by conversion of escitalopram or a derivative of formula (VI) to a salt thereof.

- 12. (previously presented): The method according to claim 10, wherein the basic ring closure is carried out by treatment with a base.
- 13. (previously presented): The method according to claim 1, wherein Hal is fluoro and R is halogen or cyano.
- 14. (previously presented): The method according to claim 1, wherein the dotted line represents a single bond.
- 15. (previously presented): The method according to claim 1, wherein Z is a dimethylaminomethyl group or a group that may be converted to a dimethylaminomethyl group.
- 16. (previously presented): The method according to claim 1, wherein the cyclic anhydride is a compound of formula (Ia).
- 17. (previously presented): The method according to claim 16, wherein the cyclic anhydride is succinic anhydride or glutaric anhydride.
- 18. (previously presented): The method according to claim 1, wherein the cyclic anhydride is a compound of formula (Ib).
- 19. (previously presented): The method according to claim 18, wherein the cyclic anhydride is phthalic acid anhydride.
- 20. (previously presented): The method according to claim 1, wherein the imide is a compound of formula (Ic).

- 21. (original): The method according to claim 20 wherein the imide is N-phenyl-succinimide substituted in the phenyl ring with a carboxy group.
- 22. (previously presented): The method according to claim 1, wherein Y in the compound of formula (IV) is a bond.
- 23. (previously presented): The method according to claim 1, wherein Y in the compound of formula (IV) is O or S.
- 24. (original): The method according to claim 23 wherein Y in the compound of formula (IV) is O.
- 25. (previously presented): The method according to claim 1, wherein Y in the compound of formula (IV) is NH.
- 26. (currently amended): The method according to claim 1, wherein  $R^1$  is selected from  $C_{1-4}$ -alkyl,  $C_{2-4}$ -alkenyl and  $C_{2-4}$ -alkynyl all of which may optionally be substituted one or more times with substituents selected from  $C_{1-4}$ -alkyl,  $C_{1-4}$ -alkylthio, hydroxy, halogen, amino, nitro, cyano,  $C_{1-4}$ -alkylamino and di- $(C_{1-4}$ -alkyl)amino.
- 27. (currently amended): The method according to claim 26 wherein  $R^1$  is selected from  $C_{1-3}$ -alkyl,  $C_{2-3}$ -alkenyl and  $C_{2-3}$ -alkynyl all of which may optionally be substituted one or more times with substituents selected from  $C_{1-3}$ -alkoxy,  $C_{1-3}$ -alkylthio, hydroxy, halogen, amino, nitro, cyano,  $C_{1-3}$ -alkylamino and di- $(C_{1-3}$ -alkyl)amino.
- 28. (original): The method according to claim 26 wherein  $R^1$  is  $C_{1\text{-4}}$ -alkyl.
- 29. (original): The method according to claim 27 wherein  $R^1$  is  $C_{1-3}$ -alkyl.
- 30. (previously presented): The method of claim 29, wherein R<sup>1</sup> is methyl, ethyl, or propyl.
- 31. (previously presented): The method according to claim 1, wherein the mixture of the compound of formula (IV) and the diol of formula (II) is prepared by selective enzymatic acylation or selective enzymatic deacylation.

- 32. (previously presented): A method for the manufacture of escitalopram, comprising the method of claim 1.
- 33. (previously presented): The method according to claim 12, wherein the base is selected from alkoxides, hydrides, or amines.
- 34. (previously presented): The method according to claim 33, wherein the base is selected from KOC(CH<sub>3</sub>)<sub>3</sub>, NaH, triethylamine, ethyldiisopropylamine, and pyridine.
- 35. (previously presented): The method according to claim 11, wherein the basic ring closure is carried out by treatment with a base.
- 36. (previously presented): The method according to claim 35, wherein the base is selected from alkoxides, hydrides, or amines.
- 37. (previously presented): The method according to claim 36, wherein the base is selected from KOC(CH<sub>3</sub>)<sub>3</sub>, NaH, triethylamine, ethyldiisopropylamine, and pyridine.
- 38. (previously presented): The method according to claim 13, wherein R is cyano.
- 39. (previously presented): The method according to claim 15, wherein Z is a dimethylaminomethyl group.
- 40. (previously presented): The method according to claim 30, wherein R<sup>1</sup> is propyl.
- 41. (previously presented): The method according to claim 1, wherein Pg is a trialkylsilyl group, benzyl group, or tetrahydropyranyl group (THP).
- 42. (previously presented): The method according to claim 1, wherein  $Pg_1$  and  $Pg_2$  are independently analysis or  $-SO_2-R^0$ , where  $R^0$  is alkyl, analysis, anylor anyl substituted with alkyl, or  $Pg_1$  and  $Pg_2$  together with the N atom to which they are attached form an optionally substituted phthalimide group.